Genomic Analysis of hESC Pedigrees Identifies De Novo Mutations and Enables Determination of the Timing and Origin of Mutational Events.

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Authors: Dalit Ben-Yosef, Francesca S Boscolo, Hadar Amir, Mira Malcov, Ami Amit, Louise C Laurent

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Public Summary:
Given the association between mutational load and cancer, the observation that genetic aberrations are frequently found in human pluripotent stem cells (hPSCs) is of concern. Prior studies in human induced pluripotent stem cells (hiPSCs) have shown that deletions and regions of loss of heterozygosity (LOH) tend to arise during reprogramming and early culture, whereas duplications more frequently occur during long-term culture. For the corresponding experiments in human embryonic stem cells (hESCs), we studied two sets of hESC lines: one including the corresponding parental DNA and the other generated from single blastomeres from four sibling embryos. Here, we show that genetic aberrations observed in hESCs can originate during preimplantation embryo development and/or early derivation. These early aberrations are mainly deletions and LOH, whereas aberrations arising during long-term culture of hESCs are more frequently duplications. Our results highlight the importance of close monitoring of genomic integrity and the development of improved methods for derivation and culture of hPSCs.

Scientific Abstract:
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